REMARKS

Applicants thank the Examiner for considering Applicants' arguments regarding traversal of the restricted subject matter and acknowledge the election of rejoined restriction groups I-III and VII consisting of Claims 1-4, 7-9, 22-24, and 27-32.

Claims 1-32 were pending in the instant application. By this amendment, claims 5-21, 25-27, 30, and 32 have been canceled without prejudice to Applicants' right to pursue the subject matter of the canceled claims in this application or other related applications. Claims 1-4, 22-24, and 28-31 have been amended, and new Claims 33-38 have been added to clarify the invention.

In particular, Applicants have amended Claims 23, 24, and 28-31 to correct antecedent language. Claims 1 and 22 have been amended to clarify the claimed method steps and their order. Support for the amendment can be found at page 16, lines 20-25; page 22, lines 14 and 23; and page 23, line 23. Claim 1 has also been amended to recite the proviso that "the specific cells do not consist of pollen cells." Support for the amendment can be found at page 21, lines 18-20. Claims 2-4 have been amended to rewrite the claims in independent form with the limitations of the Claim 1 however, the proviso added to Claim 1 has not been added as a limitation to Claims 2-4. Claims 2-4 and 24 have been amended to recite percent homology of sequences. Support for the amendment can be found at page 12, lines 10-13 of the specification. Claim 28 has been amended to clarify the role of the promoter as described in the specification. Support for the amendment can be found in the embodiments of the invention at page 19 through page 24. Claim 29 has been amended to delete "transformed by" in light of the amendment to Claims 1 and 22. Support for new Claim 33 can be found in the embodiments of the invention at page 19 through page 24. Support for new Claims 34-38 can be found at page 9, lines 1-23; page 25, lines 1-6; page 21, lines 13-15; and page 23, lines 9-15.

The amendments are fully supported by the specification and claims as originally filed, and, as such, no new matter has been added. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

The Examiner considers the title of the invention is not indicative of the invention to which the claims are directed. In response, Applicants have amended the first page of the specification to replace the title with "USES OF NUCLEIC ACIDS ENCODING POKEWEED ANTIVIRAL PROTEINS." Thus, the objection to the title has been obviated.

The Examiner has indicated that Applicants have not complied with the conditions for receiving benefit of the foreign filing date because a certified copy of the priority U.K. application has not been submitted. Applicants will submit a certified copy of the priority application in the near future.

1. OBJECTION TO THE CLAIMS

Claim 7 has been objected to as allegedly not further limiting parent Claims 2-4. In particular, the Examiner contends that "60% homologous" does not further limit "homologous" of Claims 2-4, since "homologous" is defined in the specification as sequences that are at least 70%, 80%, 90%, or 95% homologous. Applicants have canceled Claim 7, thus obviating the rejection.

Claims 27-32 are objected to for improper multiple dependency. In response, Applicants have amended Claim 29 to be dependent on any one of Claims 1, 2, 3, 4, 22, or 24, and Claims 27, 30, and 32 have been canceled. Claim 28 has been amended to depend from Claims 2, 3, 4, 22, or 24. Claim 31 has been amended to depend on Claim 4.

Claims 7-9 are objected to for certain informalities regarding incomplete sequence identifiers. Applicants have canceled Claims 7-9, rendering the objection moot.

Claims 2-4, 7-9, 23-24, and 27-28 have been objected to for certain

informalities regarding dependent form of the claims. In response, Applicants have amended Claims 23, 24, and 28 to replace "A" with "The." Claims 2-4 have been amended to be independent claims.

In view of the amendments to claims, made herein, it is submitted that this objections are avoided and moot.

2. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS, SHOULD BE WITHDRAWN

Claims 1-4, 7-9, 22-24, and 27-32 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Orthokinetic Inc. v. Safety Travel Chairs, Inc.,* 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986). Thus, according to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. *Standard Oil Co. v. American Cyanamid Co.,* 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985).

The Examiner has rejected Claims 1-4 and 22 for lacking correlation between the preamble and the method steps. The Examiner contends that the method steps are unclear and not in order, that it is unclear whether the chimaeric gene or a coding sequence comprised by the chimaeric gene encodes the PAP.

In response, Claims 1 and 22 have been amended to recite, "exposing said plant to a pathogen or chemical" or "stimulating the natural development of said plant" wherein said plant comprises the chimaeric gene. In addition, Claims 1 and 22 have been amended to recite that expression of the chimaeric gene in said specific cells induces a necrotic effect in said specific cells, in order to clarify that the steps achieve the goal recited

in the preamble. Claims 1 and 22 have also been amended to recite "a chimaeric gene comprising, a coding sequence... and a promoter" in accord with the Examiner's suggestion.

Claims 1, 22, and 28 have been rejected for the phrase "promoter which acts in response to the application of a specific stimulus to said plant." The Examiner contends that the specification fails to clarify the phrase and therefore, the metes and bounds of the claims are unclear. Applicants respectfully disagree with the Examiner's contention. In response, Claims 1 and 22 have been amended as described above to recite the limitations recited in canceled dependent Claim 27. Claims 1 and 22 have also been amended to replace the term "acts in response" with "is induced in response". The term "induced" is disclosed throughout the specification in describing promoters. For example, see page 20, line 10, wherein promoters induced upon nematode feeding are described. Thus, the metes and bounds of the claims, as amended, are definite when viewed in light of the specification.

Claims 7-9 and 27-32 have been rejected for depending upon non-elected claims. Claims 28, 29, and 31, have been amended to correct dependency and Claims 7, 27, 30, and 32 have been canceled.

Claims 22 and 28 are rejected for the recitation of the phrase "said promoter being selected to provide either nematode infection disruption, sterility, changes...or trichome development." The Examiner contends that promoters do not provide phenotypes. Claims 22 and 28 have been amended to delete the phrase. In addition, Claim 28 has been amended to clarify the invention. Claim 28, as amended, recites specific cells in which the promoter is induced. Claim 33 has been added to clarify and encompass the deleted matter of Claims 22 and 28 relating to the result of the induced necrotic effect.

Claim 31 is rejected as confusing in the recitation of the phrases "DNA isolate of a chimaeric gene" and "in combination with the method of...." The Examiner contends that the phrases are not clearly defined in the specification and hence what is encompassed by the claims is unknown.

With respect to the phrase "DNA isolate of a chimaeric gene," Applicants respectfully disagree with the Examiner's contention. The specification clearly discloses a "DNA isolate of a chimaeric gene" at page 18, line 13, in the context of the third aspect of the invention. The third aspect of the invention describes methods for isolating DNA encoding promoter sequences and incorporates by reference patents that disclosed such methods (see, for example, page 19, ¶1). Methods for isolating DNA sequences encoding PAP are also taught in the specification at page 28, ¶2. One skilled in the art would have a clear understanding of a DNA isolate of a chimaeric gene made from an isolated DNA molecule encoding a promoter and an isolated DNA molecule encoding PAP. Thus, Applicants submit that, in view of the disclosure of the specification, the phrase "DNA isolate of a chimaeric gene" has a clear and definite meaning.

Although Applicants respectfully disagree, solely in the interest of advancing prosecution, Applicants' have amended Claim 31 to be dependent on claim 4, which recites SEQ ID NO:7 that encodes the beta truncated form of PAP-S. Applicants assert that the beta truncated form of PAP-S alone was not known to exhibit necrotic function prior to the disclosure of the Applicants' experimental results.

Claims 31 and 32 are also rejected for recitation of the phrase "in combination with the method of...." In response, Applicants have amended Claim 31 to delete the phrase and canceled Claim 32.

In view of the forgoing reasoning and amendments, Applicants respectfully request the Examiner's withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

3. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 1-4, 7-9, and 27-32 have been rejected under 35 U.S.C. 112, first paragraph, because the specification allegedly does not reasonably provide enablement for a method that employs "any part" of a mature PAP or a coding sequence that is homologous and having the same functionality of the disclosed sequences to induce resistance.

According to applicable case law, under 35 U.S.C. § 112, where a disclosure provides considerable direction and guidance on how to practice the invention and presents working examples, and where, at the time of application, the skill in the art was quite high and the methods needed to practice the invention well known, a conclusion of enablement should be made. *In re Wands*, 858 F.2d 731, 740, 8 U.S.P.Q.2d. 1400, 1406 (Fed. Cir. 1988). Therein, eight factors for consideration in determining enablement are set forth (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.*

Contrary to the Examiner's contention, one skilled in the art, could follow the teachings of the specification to determine if parts of or homologous sequences of a PAP-encoding nucleotide sequence exhibit the desired function without undue experimentation. First, Applicants submit that techniques for plant transformation and the skills in molecular biology needed to select an appropriate PAP sequence following the teachings of the specification are well known in the art. Given that the level of skill in very high in this field and that the specification has provided ample guidance on how to practice the methods, no undue experimentation is required for the skilled person to practice the invention. (Furthermore, exposing the transgenic plant of the method of the invention to a pathogen or a chemical or stimulating the natural development of said plant requires no particular skill

beyond that possessed by one skilled in the art.)

In the present instance, the specification provides ample direction and guidance for one skilled in the art to choose or make a nucleotide sequence that encodes a PAP that induces a necrotic effect. For example, certain domains of PAP sequences critical for PAP function are disclosed in the abridging ¶ on pages 40 and 41, wherein structural features of the PAP α domain and the PAP β domain are discussed. The PAP α domain is described as including the RNA recognition motif and ribosome binding regions, and the PAP β domain is described as containing a critical catalytic residue site and having an active folded conformation. One skilled in the art would recognize and use the information regarding such domains in choosing PAP sequences that could be used in the methods of the invention.

The specification also teaches specific primers that could be used in making a nucleic acid sequence comprising domains having the desired function. For example, see page 29, lines 1-3, and page 28, lines 7-9, wherein primers for the α and β domains of PAP are disclosed which are based on an alignment of PAP-S and divergent maize RIPs. One skilled in the art could use such primers to isolate and manipulate PAP α and β domains from different organisms. The specification also discloses methods "to screen for similar sequences," to the disclosed PAP encoding sequences using methods common in that art, such as nucleic acid hybridization, *e.g.*, see page 11, line 16 through page 12, line 10. An invention is enabled even though the disclosure may require some routine experimentation to practice the invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Thus, given the nature of the claimed methods and the amount of guidance disclosed in the specification, one skilled in the art can obtain functional PAP sequences for use in the methods of the invention without undue experimentation.

The Examiner contends that the ability of any PAP sequence to assert antiviral activity and/or nematode resistance in plant cells cannot be extrapolated to sequences coding

for "any part" of any mature PAP or homologous sequences of the disclosed sequences of the invention. Applicants respectfully point out that the claimed methods are not specifically directed to the antiviral activity or nematode resistance of PAP *per se*, but rather the induction of necrotic effects in plant cells. Such necrotic effects can be assessed without undue experimentation. Following the teachings of the specification, one skilled in the art could easily determine if a PAP sequence induced a necrotic effect.

The Examiner's attention is drawn to page 17, ¶3 wherein necrotic effects are described, and page 18, ¶1, wherein "lethal effect" is disclosed and such "effects" are further defined in the context of PAP protein expression. One skilled in the art would be able to use the experimental examples of assays disclosed in the specification to identify PAP with necrotic effects. For example, at page 40, ¶1, the assays of PAP expression in tobacco plant cells showed inhibition of protein translation which is directly linked to necrosis of specific cells. Another example at page 49 and 50 shows that transgenic potatoes expressing Pro-PAP-S exhibit nematode resistance. The specification also discloses transformation of plant cells with PAP constructs along with GUS reporter constructs to determine function, *e.g.*, see page 38, line 18 through page 39, line 10.

The Examiner contends that the breadth of the claims has not been enabled in that Applicants have allegedly not taught that <u>any</u> part of a mature PAP encoding sequence and <u>all</u> sequences that are at least 60%, 70%, and 80% homologous to the disclosed sequences are capable of inducing necrotic effect in specific cells of a plant. Applicants respectfully disagree and submit that, in accord with case law, an inventor is not required to disclose "a test of <u>every</u> species encompassed by their claims" even in an unpredictable art. <u>In re Angstadt</u>, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976) (emphasis in original). Moreover, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. *Atlas Powder Co. v E. I. Du Pont* 750 F2d. 1569. The standard is whether a skilled person could determine which embodiments that were conceived, but not

yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Id.* Also see MPEP 2164.08(b). In the present case, one skilled in the art would readily be able to determine which PAP sequences would be inoperative or operative in inducing a necrotic effect. As described above, with expenditure of no more effort than is normally required in the art, the skilled artisan would be able to determine if a nucleic acid molecule encoding a PAP sequence or homologue or portion thereof has the desired function, and therefore can be used in the methods of the invention.

Applicants submit that several working examples have been provided in the specification to enable the invention. The illustrative examples, as indicated by the Examiner, include pro-PAP, mature-PAP-S, PAP-S α and PAP-S β encoding sequences. The specification discloses another example, a PAP-S PCR product, at page 28, ¶2. Mature-PAP, PAP α, and PAP β are homolgous to the pro-PAP sequence from which they are derived. Similarly, PAP α and PAP β are homolgous to mature-PAP. Mature-PAP-S, PAP-S α and PAP-S β encoding sequences fall within the meaning of a 'part' of, or homologous to, a PAP sequence, since they are at least 70% homologous to the pro-PAP sequence. Experimental results disclosed in the specification exemplify how PAP sequences can be tested for the desired function, *e.g.,* see page 44, ¶2 and Figures 6 and 7. Therein, pro-PAP-S and PAP-S sequences were found to inactivate translation which is indicative of the sequences' ability to induce a necrotic effect, since inhibition of translation leads to necrosis. Thus, the specification discloses working examples of homologous sequences having the desired function that can be used in the methods of the invention. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The Examiner also cites unpredictability of the phytotoxicity of PAP expressed in transgenic plants as evidence that one skilled in the art would not be able to

make and use the claimed methods of the invention. Applicants disagree and point out that while varying degrees of deleterious toxic effects were observed in some instances in the prior art, these instances were limited to transgenic plants comprising PAP sequence linked to promoters that are constitutively expressed in plants, such as the 35S RNA promoter from CMV and the ubiquitin promoter. See Lodge *et al.* (1993, Proc. Natl. Acad. Sci. USA 90:7089-7093) page 7089, second column, ¶3. Applicants submit that the present invention is fundamentally different from constitutive expression of PAP wherein the metabolism of every plant cell is altered as a result of the presence of PAP throughout the plant. One skilled in the art would recognize that numerous physiological processes in the plant would be affected and contribute to the deleterious effects in the prior art plants. The prior art teachings differ from limited PAP expression in specific cells where metabolism of the whole plant is not altered dramatically. Thus, the unpredictability of PAP phytotoxicity associated with constitutive expression of a PAP, cited by the Examiner, is different and not relevant to the localized necrotic effect of PAP expression in specific cells. Moreover, in many instances, the exposure and stimulus of the methods of the present invention would be localized to a specific portion of a plant, and not lead to toxic effects throughout the plant. In other instances, the promoters for use in the invention exhibit expression patterns limited to specific cells, which would not produce toxic effects in the entire plant. Thus, the unpredictability of the art alleged by the Examiner as a factor in determining enablement of the claimed method is not applicable to the claimed methods.

The teachings and working examples of the instant specification would clearly enable one to practice the steps of the claimed methods of the invention for inducing necrotic effect in specific cells of a plant without requiring undue experimentation. In light of the foregoing reasoning, the rejection under 35 U.S.C. § 112, first paragraph for lack of enablement should be withdrawn.

4. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 1-4, 7-9, and 27-32 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner contends that the specification does not provide written description support for sequences having the same functionality as the disclosed mature PAP sequences or sequences having at least 60%, 70%, and 80% homology. Furthermore, the Examiner contends that the specification does not describe methods that use said nucleic acid sequences and plants and plant cells produced by said methods.

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, pages 1099-1111), specifies that:

> " Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidenced of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function and the method of making the claimed invention." *Id.* at page 1106, column 2, lines 25-41.

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

Furthermore, in accord with the Written Description Guidelines, what is

conventional or well known to one of skill in the art need not be disclosed in detail and where the level of knowledge and skill in the art is high a written description questions should not be raised (Fed. Reg. Vol. 66, no. 4, January 5, 2001, p. 1106).

In the present instance, Applicants have disclosed representative examples of PAP encoding sequences that induce a necrotic effect, the level of skill and knowledge in the art related to PAP sequences is high, and the specification describes techniques that can be use din practicing the claimed methods.

Examples of PAP sequences disclosed in the specification suitable for use in the methods of the invention are discussed above in response to the enablement rejection. Mature-PAP, PAP α, and PAP β are homolgous to the pro-PAP sequence from which they are derived. Similarly, PAP α and PAP β are homolgous to mature-PAP. The specification teaches aligning of sequences and examining the number of positions with exact nucleotide correspondence at page 28, ¶2. It is clear from the examples presented in the specification that "homology" means percent identity, meaning a measure of the relationship between two polypeptide sequences or two polynucleotide sequences, as determined by comparing their sequences. Applicants submit that the high level of knowledge and the presence of PAP sequences in the art coupled with the PAP examples provided in the specification are sufficient to show that Applicants were in possession of the claimed invention.

The claimed methods for inducing a necrotic effect in specific plant cells are clearly described in the specification. Methods for identifying coding sequences for PAP having the desired necrotic effect are disclosed in the specification as described above in the response to the enablement rejection. Techniques for expressing such sequences in a specific cells of a plant are also disclosed and were commonly known to those skilled in the art. Since one skilled in the art can perform the methods with ease and the specification provides adequate examples, it is clear that Applicants were in possession of the claimed methods. Thus, a skilled artisan would have understood the inventor to be in possession of the claimed

invention at the time of filing, given the description of the methods in the specification and the numerous PAP sequences available in the art.

In addition, not only does the specification describe ways to identify PAP having desired functional characteristics, these functional characteristics are correlated with structure. For example, abridging ¶ on pages 40 and 41 describes structural predictions of the PAP α domain as containing the RNA recognition motif and ribosome binding regions and the PAP β domain as containing a critical catalytic residue site and having an active folded confirmation. This disclosure directly correlates the structure of PAP to the desired function of PAP, *i.e.,* inhibition of protein translation, which in turn results in necrotic effects. In accord with the Written Description guidelines, such evidence of a correlation between structure and function is an additional supporting factor of the adequacy of written description support in the specification.

Applicants submit that the disclosure of the specification, in view of the state of the art, is sufficient to show the applicant was in possession of the claimed PAP sequences, parts and homologues thereof that cause necrotic effects, for use in the methods of the invention.

In light of the foregoing reasoning and amendments, the rejection under 35 U.S.C. § 112, first paragraph for lack of written description support should be withdrawn.

5. THE REJECTION UNDER 35 U.S.C. § 102(b) FOR ANTICIPATION SHOULD BE WITHDRAWN

Claims 1 and 27-28 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Baszczynski *et al.* (U.S. patent no. 5,756,324, "Baszczynski"). The Examiner contends that Baszczynski teaches a method of inducing viral resistance in a plant by expressing a structural gene encoding PAP under the control of the Bnm1 promoter, a microspore specific promoter. Furthermore, the Examiner contends that since PAP is expressed in the microspore cells of the plant, necrotic effect is inherently induced in said

cells.

Anticipation under 35 U.S.C. § 102 requires identity of invention. The court made it absolutely clear that "anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference ... [and] ... [t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person or ordinary skill in the field of the invention." *Scripps Clinic & Research Fdn. v. Genentech Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

Baszczynski's invention relates to the use of a microspore-specific regulatory element for production of virus and insect resistant plants. In one of several different approaches to protect plants from diseases, Baszczynski discloses use of a microspore-specific regulatory element to express PAP (see, Section 5, column 17, lines 1-24). Separately, Section 4 of Baszczynski, beginning at column 11, line 37, describes antisense, ribozyme, and mRNA cleavage methods for achieving male-sterile transgenic plants. Baszczynski does not disclose use of PAP encoding sequences for the purpose of producing male-sterile plants.

Claim 1 has been amended to recite the proviso that the specific cells do not consist of pollen cells[1]. Since microspore cells are developing pollen cells, and thus a type of pollen cell, Claim 1, as amended, does not encompass induction of PAP expression in a microspore-specific manner. Thus, Claim 1, as amended, and dependent claims thereon are not anticipated by the teachings of Baszczynski.

Claims 2, 3, and 4 have been amended in order to rewrite the claims in

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[1] The Examiner's attention is respectfully invited to MPEP 2173.05(i), wherein the criteria for support of a proviso is described as:

> "Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." *In re Johnson*, 558 F.2d 1008, 1019, 194 U.S.P.Q. 187, 196 (CCPA 1977).

Applicants assert that the genus of targeted cells provides sufficient support for the amendment adding the proviso. Examples of targeted cells disclosed in the specification include, pollen, anther, and tapetum, *e.g.*, see page 21, ¶3.

independent form with the limitations of Claim 1. The claims as amended do not encompass the methods taught by Baszczynski, because Baszczynski teaches transforming plants to express PAP as described by Lodge *et al.*, which is isolated from leaves, *e.g.*, see Lodge *et al.*, page 7089, second column. Applicants point out that Claims 2, 3, and 4 are directed to methods for inducing necrosis in specific cells by expressing sequences encoding PAP-S (from seed) and thus do not encompass Baszczynski's teaching of using only PAP from leaf.

In addition, Claim 2 has been amended to recite that the coding sequence is at least 80% homologous to SEQ ID NO:3 (nucleic acid sequence encoding a mature PAP-S) and the amino acid sequence is at least 90% homologous to SEQ ID NO:4. The PAP described by Lodge *et al.*, is less than 90% homologous to PAP-S, and thus the homologs of PAP-S would not encompass the leaf-derived PAP taught by Lodge *et al.* and Baszczynski. With respect to Claims 3 and 4, Baszczynski does not teach use of PAP α or β truncated forms. Thus, Claims 2, 3, and 4, as amended, are not anticipated by Baszczynski.

In view of the amendments to the claims and the reasoning presented above, Baszczynski does not disclose the claimed invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C.§ 102(b) be withdrawn.

6. THE REJECTION UNDER 35 U.S.C. § 102(b) OR 103(a) FOR ANTICIPATION OR OBVIOUSNESS SHOULD BE WITHDRAWN

Claims 29-32 have been rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Tumer (U.S. patent no. 5,880,329).

The Examiner alleges that Tumer teaches transgenic plants and plant cells produced by a method comprising transforming a plant or plant cells with a chimeric gene comprising a DNA encoding a mature wild type PAP or PAP mutant and an inducible, constitutive, or tissue-specific promoter, wherein the expressed PAP induces viral resistance in the transformed plant.

Applicants point out that the purpose of Tumer's experiments are to identify mutant PAP-encoding genes that exhibit the antiviral activity of wild type PAP but do not exhibit the phytotoxicity of wild type PAP. Tumer's goal is achieved by screening for mutant PAP with "reduced phytotoxicity" which is defined as producing a normal fertile phenotype rather than a stunted or molted phenotype, *i.e.,* toxic effects, when expressed in a plant (see column 2, line 65 through column 3, line 2).

Contrary to the Examiner's allegation, Tumer does not disclose transforming plants with wild type PAP. In fact, the examples of plant transformation disclosed in Tumer are limited to transformation using the constructs of plasmids NT144, NT145, NT146, NT147, and NT168, all of which contain nucleic acid sequences encoding non-toxic mutant PAP, *e.g.*, see abridging ¶ of columns 15 and 16, and example sections 2-5, at columns 15-22. Tumer does not disclose transforming a plant with a chimaeric gene comprising a mature PAP sequence, nor does Tumer disclose transforming a plant with a PAP encoding sequence capable of causing necrosis in specific cells. The plants, chimaeric genes, and recombinant plant cells disclosed by Tumer also lack the necrosis-inducing PAP sequences found in the plants, chimaeric genes, and recombinant plant cells of the methods of the invention. Tumer does not disclose each and every element of the claimed method, and therefore does not meet the requirements for anticipation.

A finding of obviousness under 35 U.S.C. §103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). Stated differently, for a claimed invention to be deemed obvious in view of a prior art disclosure, the prior art disclosure must, firstly, give rise to a suggestion of or motivation for the claimed subject matter.

Applicants assert that the methods of Claims 29-32 are not rendered obvious by the disclosure of Tumer. Tumer does not suggest the claimed invention as it teaches transforming plants with PAP sequences that have anti-viral and anti-fungal activities, but lack the ability to induce a toxic, *i.e.*, necrotic effect. Tumer generally describes assessing the antiviral effects of PAP, *e.g.*, see, column 11, lines 27-59. Observations of deleterious effects in transgenic plants expressing PAP are presented as problems to be overcome, not benefits that can be used to achieve the goal of inducing a necrotic effect, *e.g.*, column 1, lines 62-67. In effect, Tumer's disclosure teaches away from the claimed invention. Tumer does not give rise to a suggestion of the claimed subject methods of the invention and therefore does not make obvious the claimed methods.

Moreover, the PAP mutants of Tumer do not produce toxic effects in the plants transformed as described at column 16, lines 60-67, and column 19, line 19. In contrast, a toxic effect would be a requisite element for a PAP to achieve the necrotic effect that is the goal of the claimed methods of the present invention. One skilled in the art would not find a reasonable expectation that the mutant PAP sequences used in transforming plants in Tumer would achieve the goal of inducing a necrotic effect in specific plant cells.

Applicants submit that the rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) are in error, and respectfully request that the rejections be withdrawn.

7. THE REJECTION UNDER 35 U.S.C. § 103(a) FOR OBVIOUSNESS SHOULD BE WITHDRAWN

Claims 1-4, 7-9, 22, and 27-32 have been rejected under 35 U.S.C. § 103(a) as obvious over Kanieswski *et al.* (U.S. patent no. 6,015,940, hereafter "Kanieswski").

The Examiner contends that it would have been obvious to one of ordinary skill in the art to use the method of transforming a plant with pokeweed antiviral protein encoding DNA to induce viral resistance as taught by Kanieswski and to modify that method by incorporating any other PAP-encoding DNA sequence with any other suitable regulatory

element to induce viral resistance in a plant or in specific cells of the plant as suggested by Kanieswski.

A rejection for obviousness is improper when there is nothing in the cited prior art references, either singly or in combination, to suggest the desirability of the claimed subject matter. For a rejection of claimed subject matter as obvious in view of a combination of prior art references to be upheld, (1) the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or use the claimed method, as the case may be; and (2) the prior art must have revealed that in so doing, those of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

In the present instance, Kanieswski provides neither a suggestion of the claimed methods, nor a reasonable expectation of success that a necrotic effect can be induced in specific cells using a PAP encoding sequence expressed in a transgenic plant. Kanieswski's goal is to provide viral resistance to potato plant and tuber by expressing a PAP-encoding sequence. The sequence encodes a PAP with antiviral activity and expression is directed to "certain cell types where virus infection can occur." (see, column 9, lines 36 and 37).

As is the case in Tumer, the focus of Kanieswski is to express PAP in a manner that imparts viral resistance, but does not result in necrosis of specific cells where PAP is expressed. Kanieswski states that, "[T]the particular promoter selected is preferably capable of causing sufficient expression to result in the production of an effective amount of pokeweed antiviral protein to prevent virus infection, but not such as to be detrimental to the potato cell." See Column 9, lines 38-41. In contrast, the instant specification teaches expression of PAP to achieve necrosis such that, "a lethal or detrimental effect is produced in, and only in, the specific cells." See page 17, ¶3. Thus, there is no suggestion in Kanieswski

to direct PAP expression to specific cells to achieve necrosis in specific cells of a plant.

In fact, Kanieswski teaches the opposite of the claimed invention. Kanieswski's goal of achieving viral resistance requires that the potato cells, including tuber cells, exhibit protection against viral infection and do not die as a result of the infection, whereas the claimed methods encompass necrotic, *i.e.,* lethal and deleterious effects, on specific cells. The requisite suggestion to express toxic PAP in a plant is clearly not present in Kanieswski.

As stated in the Office Action at page 14, line 17, "Kanieswski *et al.* does not expressly teach inducing necrotic effect in specific cells of the plant." Applicants submit that the Examiner has apparently engaged in hindsight reconstruction, while attempting to combine distinct portions of the prior art, *i.e.*, different types of promoters and cytotoxic effects of PAP, with the teachings of the Applicants to arrive at the claimed method. Without the teachings of the present application, the claimed method could not have been foreseen by a person of ordinary skill in the art, since there was no suggestion of it in the art and their utilities based on inducing necrosis in specific plant cells could not have been envisaged. The Federal Circuit has made very clear that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, at 1075, U.S.P.Q.2d 1596 (Fed. Cir. 1988).

Applicants submit that the rejection under 35 U.S.C. § 103(a) is in error, and respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants respectfully request that the foregoing amendments and remarks be made of record in the file history of the instant application. Applicants believe that the remarks and amendments made herein now place the pending claims in condition for allowance. It is believed that no fee is required for filing this Amendment. In the event a fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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Enclosures